AMENDMENTS

AMENDMENTS TO THE CLAIMS

In the Claims:

1. (Currently amended) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising mammalian cultured cells or a non-human animal expressing a MBM polypeptide or nucleic acid, wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system[[;]] , ~~and~~

~~(d) comparing the~~ wherein a difference between the test agent-biased activity and the reference activity ~~to determine whether~~ identifies the test agent as ~~is~~ a candidate branching morphogenesis modulating agent[[;]] , and wherein the MBM polypeptide or nucleic acid is ~~selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6,~~ MAPK4~~, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG~~.

2. (Cancelled)

3. (Cancelled)

4. (Currently amended) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a MBM polypeptide or nucleic acid;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system[[;]] , ~~and~~

~~(d) comparing the~~ wherein a difference between the test agent-biased activity and the reference activity ~~to determine whether~~ identifies the test agent as ~~is~~ a candidate branching morphogenesis modulating agent[[;]] , wherein the MBM polypeptide or nucleic acid is

~~selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6,~~ MAPK4, ~~NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG,~~ and wherein the assay system includes a binding assay comprising a ~~MBM~~ MAPK4 polypeptide and the candidate test agent is an anti-MAPK4 antibody.

5. (Currently amended) The method of Claim 1 wherein the assay system includes an expression assay comprising a ~~MBM~~ MAPK4 nucleic acid and the candidate test agent is a nucleic acid modulator.

6. (Currently amended) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a MBM polypeptide or nucleic acid;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system; ~~and~~

~~(d) comparing~~ wherein the difference between the test agent-biased activity and the reference activity ~~to determine whether~~ identifies the test agent as ~~is~~ a candidate branching morphogenesis modulating agent[[;]] , wherein the MBM polypeptide is ~~selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6,~~ MAPK4, ~~NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG~~[[;]] and wherein the assay system includes an expression assay comprising a ~~MBM~~ MAPK4 nucleic acid[[;]] and the candidate test agent is ~~a nucleic acid modulator; and wherein the nucleic acid modulator is~~ an antisense oligomer against MAPK4.

7. (Currently Amended) The method of Claim 6 wherein the ~~nucleic acid modulator~~ antisense oligomer is a phosphorodiamidate morpholino oligonucleotide (PMO).

8. (Cancelled)

9. (Currently amended) The method of Claim ~~8~~ 1, wherein the branching morphogenesis is angiogenesis.

10. (Currently amended) The method of Claim ~~8~~ 1, wherein the assay system comprises cultured cells.

11. (Original) The method of Claim 10 wherein the assay detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

12. (Original) The method of Claim 10 wherein the assay detects tubulogenesis or cell migration or cell sprouting, and wherein the assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

13. (Original) The method of Claim 10 wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.

14. (Currently amended) The method of Claim ~~8~~ 1, wherein the assay system comprises a non-human animal.

15. (Original) The method of Claim 14 wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.

16. (Original) The method of Claim 15 wherein the assay system includes a transgenic tumor assay that includes a mouse comprising a RIP 1-Tag2 transgene.

17. (Currently amended) The method of Claim 1, comprising the additional steps of:

(d) providing a second assay system comprising mammalian cultured cells or a non-human animal expressing MBM, wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis;

(e) contacting the second assay system with the test agent of (b) or an agent derived therefrom under conditions whereby, but for the presence of the test agent or agent derived therefrom, the system provides a reference activity; and

(f) detecting an agent-biased activity of the second assay system, wherein a difference between the agent-biased activity and the reference activity of the second assay system confirms the test agent or agent derived therefrom as a candidate branching morphogenesis modulating agent~~, and wherein the second assay system includes a second assay that detects an agent-biased change in an activity associated with branching morphogenesis~~.

18. (Currently amended) The method of Claim 17 wherein the second assay detects an agent-biased change in an activity associated with angiogenesis.

19. (Original) The method of Claim 17 wherein the second assay system comprises cultured cells.

20. (Original) The method of Claim 19 wherein the second assay detects an event selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

21. (Original) The method of Claim 20 wherein the second assay detects tubulogenesis or cell migration or cell sprouting, and wherein the second assay system comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

22. (Original) The method of Claim 20 wherein the assay detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.

23. (Original) The method of Claim 17 wherein the assay system comprises a non-human animal.

24. (Original) The method of Claim 23 wherein the assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.

25. (Original) The method of Claim 24 wherein the assay system includes a transgenic tumor assay that includes a mouse comprising a RIP1-Tag2 transgene.

26. – 32. (Cancelled)

33. (New) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising mammalian cultured cells or a non-human animal expressing a MBM polypeptide or nucleic acid, wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent, and wherein the MBM polypeptide or nucleic acid is selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG.

34. (New) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a MBM polypeptide or nucleic acid;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate branching morphogenesis modulating agent; wherein the MBM polypeptide or nucleic acid is selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG, and wherein the assay system includes a binding assay comprising a MBM polypeptide and the candidate test agent is an antibody.

35. (New) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a MBM polypeptide or nucleic acid;

(b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and

(c) detecting a test agent-biased activity of the assay system, wherein the difference between the test agent-biased activity and the reference activity identifies the test agent as is a candidate branching morphogenesis modulating agent; wherein the MBM polypeptide is selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG; and wherein the assay system includes an expression assay comprising a MBM nucleic acid and the candidate test agent is an antisense oligomer.

36. (New) A method of identifying a candidate branching morphogenesis modulating agent, said method comprising the steps of:

(a) providing a first assay system comprising cultured mammalian cells expressing a MAPK4 polypeptide or nucleic acid;

(b) contacting the cultured mammalian cells with a test agent;

(c) measuring the activity of the MAPK4 polypeptide or the expression of the MAPK nucleic acid in the cultured mammalian cells, wherein a difference between the activity or expression of the MAPK4 polypeptide or nucleic acid in the presence of the test agent compared to its absence identifies the test agent as a candidate branching morphogenesis modulating agent;

(d) providing a second assay system comprising cultured mammalian cells or a non-human animal expressing a MAPK4 polypeptide or nucleic acid capable of detecting a change in activity associated with branching morphogenesis;

(e) contacting the second assay system with the test agent of (b) or an agent derived therefrom; and

(f) measuring the activity associated with branching morphogenesis in the cultured cells or the non-human animal, wherein a difference between the activity associated with branching morphogenesis in the presence of the test agent or agent derived therefrom compared to its absence confirms the test agent as a candidate branching morphogenesis modulating agent.

37. (New) The method of Claim 36, wherein the second assay system detects an activity selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions.

38. (New) The method of Claim 37, wherein the second assay system detects tubulogenesis or cell migration or cell sprouting, and comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents.

39. (New) The method of Claim 37, wherein the second assay system detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent.

40. (New) The method of Claim 36, wherein the second assay system comprises a non-human animal.

41. (New) The method of Claim 40, wherein the second assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay.

42. (New) The method of Claim 41, wherein the second assay system includes a transgenic tumor assay that includes a mouse comprising a RIP 1-Tag2 transgene.